

AMENDMENTS TO THE CLAIMS

This listing of claims replaces all prior listings or versions of claims in this application:

Claims 1-43 (Canceled)

44. (Previously presented) A double-stranded ribonucleic acid (dsRNA), consisting of first and second single RNA strands, wherein the first single RNA strand is an antisense RNA strand, the second single RNA strand is a sense RNA strand, wherein the antisense RNA strand is complementary to a target gene or a portion thereof, the dsRNA having increased effectiveness in inhibiting the expression of a target gene by means of RNA interference, wherein the dsRNA comprises first and second double-stranded ends and at least one single-stranded overhang which is 2 to 4 nucleotides in length, wherein the unpaired nucleotide of the single-stranded overhang that is directly adjacent to the terminal nucleotide base pair comprises a purine base, wherein a single-stranded overhang is located at the 3'-end of the antisense strand, wherein the overhang comprises the sequence 5'-GC-3'; and wherein the terminal base pair of the first double-stranded end comprises a guanine-cytosine (G-C) base pair or the four consecutive terminal base pairs of the first double-stranded end comprises at least two G-C base pairs; wherein the terminal base pair of the second double-stranded end comprises a guanine-cytosine (G-C) base pair or the four consecutive terminal base pairs of the second double-stranded end comprises at least two G-C base pairs; excluding the following dsRNAs:

5'- CAGGACCUCGCCGCGUCAGACC-3' (SEQ ID NO: 1)

3'-CGGUCCUGGAGCGGCGACGUCUGG-5' (SEQ ID NO: 2),

5'- UGCAGCUUCGAAGCCUCACAGA-3' (SEQ ID NO: 27)

3'-CGACGUUCGAAGCUUCGGAGUGU-5' (SEQ ID NO: 28), and

5'- UGGGGAGAGAGUUCUGAGGAUU-3' (SEQ ID NO: 29)

3'-CGACCCCUCUCUCAAGACUCCU-5' (SEQ ID NO: 30).

45. (Previously presented) The dsRNA of claim 44, wherein each nucleotide overhang independently consists of 2 unpaired nucleotides.
46. (Previously presented) The dsRNA of claim 44, wherein at least half of the unpaired nucleotides comprise a purine base.
47. (Previously presented) The dsRNA of claim 44, wherein the unpaired nucleotide adjacent to the terminal nucleotide base pair comprises a guanine (G).
48. (Previously presented) The dsRNA of claim 44, wherein the unpaired nucleotide adjacent to the terminal nucleotide base pair comprises an adenine (A) base.
49. (Previously presented) The dsRNA of claim 44, wherein said nucleotide overhang comprising the sequence 5'-GC-3' consists of the sequence 5'-GC-3'.
50. (Previously presented) The dsRNA of claim 44, wherein the region of the antisense strand that is complementary to the target gene is 19 to 24 nucleotides in length.
51. (Previously presented) The dsRNA of claim 44, wherein the antisense strand is 20 to 28 nucleotides in length.
52. (Previously presented) The dsRNA of claim 44, wherein the antisense strand is 21 nucleotides in length.
53. (Previously presented) The dsRNA of claim 44, wherein at least one of the RNA strands comprises at least one chemically modified nucleotide.
54. (Previously presented) The dsRNA of claim 53, wherein the chemically modified nucleotide comprises a non-natural base.

55. (Previously presented) The dsRNA of claim 53, wherein the chemically modified nucleotide comprises a 2' modification.
56. (Previously presented) The dsRNA of claim 55, wherein the 2' modification is selected from the group consisting of a 2'-amino modification, a 2'-alkyl modification, a 2'-O-methyl modification, a 2'-O-ethyl modification, a 2'-O-propyl modification, a 2'-O-allyl modification, a 2'-O-aminoalkyl modification, and a 2'-deoxy-2'-fluoro modification.
57. (Withdrawn) A method for the targeted selection of a double-stranded ribonucleic acid (dsRNA), consisting of first and second single RNA strands, wherein the first single RNA strand is an antisense RNA strand, the second single RNA strand is a sense RNA strand, wherein the antisense RNA strand is complementary to a target gene or a portion thereof, the dsRNA having increased effectiveness in inhibiting the expression of a target gene by means of RNA interference, comprising the steps of:
- (a) selecting a dsRNA comprising first and second double-stranded ends and at least one single-stranded overhang which is 2 to 4 nucleotides in length;
 - (b) selecting a dsRNA comprising first and second double-stranded ends, wherein the unpaired nucleotide of the single-stranded overhang that is directly adjacent to the terminal nucleotide base pair comprises a purine base, wherein a single-stranded overhang is located at the 3'-end of the antisense strand, and wherein the overhang comprises the sequence 5'-GC-3'; and
 - (c) selecting a dsRNA comprising first and second double-stranded ends, wherein the terminal base pair of the first double-stranded end comprises a guanine-cytosine (G-C) base pair or the four consecutive terminal base pairs of the first double-stranded end comprises at least two G-C base pairs; wherein the terminal base pair of the second double-stranded end comprises a guanine-cytosine (G-C) base pair or the four consecutive terminal base pairs of the second double-stranded end comprises at least two G-C base pairs;
- excluding the following dsRNAs:

5'- CAGGACCUCGCCGCGCAGACC-3'	(SEQ ID NO: 1)
3'-CGGUCCUGGAGCGGCGACGUCUGG-5'	(SEQ ID NO: 2),
5'- UGCAGCUUCGAAGCCUCACAGA-3'	(SEQ ID NO: 27)
3'-CGACGUCCAAGCUUCGGAGUGU-5'	(SEQ ID NO: 28), and
5'- UGGGGAGAGAGUUCUGAGGAUU-3'	(SEQ ID NO: 29)
3'-CGACCCCUCUCUCAAGACUCCU-5'	(SEQ ID NO: 30).

58. (Withdrawn) The method of claim 57, wherein each nucleotide overhang independently consists of 2 unpaired nucleotides.
59. (Withdrawn) The methods of claim 57, wherein at least half of the unpaired nucleotides comprise a purine base.
60. (Withdrawn) The method of claim 57, wherein the unpaired nucleotide adjacent to the terminal nucleotide base pair comprises a guanine (G) base.
61. (Withdrawn) The method of claim 57, wherein the unpaired nucleotide adjacent to the terminal nucleotide base pair comprises an adenine (A) base.
62. (Withdrawn) The method of claim 57, wherein said nucleotide overhang comprising the sequence 5'-GC-3' consists of the sequence 5'-GC-3'.
63. (Withdrawn) The method of claim 57, wherein the region of the antisense strand that is complementary to the target gene is 19 to 24 nucleotides in length.
64. (Withdrawn) The method of claim 57, wherein the antisense strand is 20 to 28 nucleotides in length.

65. (Withdrawn) The method of claim 57, wherein the antisense strand is 21 nucleotides in length.
66. (Withdrawn) The method of claim 57, wherein at least one of the RNA strands comprises at least one chemically modified nucleotide.
67. (Withdrawn) The method of claim 66, wherein the chemically modified nucleotide comprises a non-natural base.
68. (Withdrawn) The methods of claim 66, wherein the chemically modified nucleotide comprises a 2' modification.
69. (Withdrawn) The method of claim 68, wherein the 2' modification is selected from the group consisting of a 2'-amino modification, a 2'-alkyl modification, and a 2'-O-methyl modification, a 2'-O-ethyl modification, a 2'-O-propyl modification, a 2'-O-allyl modification, a 2'-O-aminoalkyl modification, and a 2'-deoxy-2'-fluoro modification.
70. (Previously presented) A pharmaceutical composition for inhibiting the expression of a target gene by means of RNA interference, comprising a dsRNA of claim 44, or a salt, prodrug or hydrate thereof; and a pharmaceutically acceptable carrier.
71. (Withdrawn) A method for inhibiting the expression of a target gene in a cell, comprising:
 - (a) introducing into the cell a dsRNA of claim 44, or a salt, prodrug or hydrate thereof; and
 - (b) maintaining the cell for a time sufficient to obtain degradation of a mRNA transcript of the target gene.
72. (Withdrawn) The method of claim 71, wherein the cell is a mammalian cell.

73. (Withdrawn) The method of claim 72, wherein the cell is a human cell.
74. (Withdrawn) The method of claim 71, wherein the target gene is selected from the group consisting of 11-hydroxysteroid dehydrogenase-1, acetyl-CoA-carboxylase-2, acyl CoA : DAG acyltransferase-1, Adenosine A2 receptor, akt, AML-ETO, amyloid beta precursor protein (APP), ApoA1, ApoB, ApoM, APS (adaptor protein with pleckstrin homology and src homology 2 domains, a-synuclein, Aurora A, Aurora B, beta-1 integrin subunit, beta-amyloid converting enzyme (BACE), Bax, beta-catenin, Bcl2, Bcl-XL, Bcr- abl, caspase 8, caspase-3, C CR2, CD40, CD40L, cdk2, chk1, chk2, clottingfactorVII, collagen, CD132, CTLA4, cyclin E, Dhcr24, Dipeptidylpeptidase-IV, E-Cadherin, Eg5/KSP, EGF, EGFR1, EWS-Flil, FAS-fatty acid synthase, FoxA-3, FoxO-1, Fructose-1,6-bisphosphate, Glucose-6-phosphate, GM3 synthase, HDAC (histone deacetylase 1-6,9), Her-2/erb2, HIF1, HMG CoA reductase, hormone sensitive lipase, huntingtin, IKK1, IKK2, LDLR, MDR1, Microsomal Triglyceride Transfer Protein, MMP1, MMP2, MMP9, MyD88, sodium voltage gated type X alpha polypeptide (Nav1. 8), NFkB, p38 map kinase mitogen activated protein kinase, p85a regulatory subunit of PI3-kinase, PEPCK, plkl, PTEN, PTP-1B, PU. 1, raf, ras, Resistin, SCAP, SERBP-2, SHIP-2, SMAD7, SREBP1C, STAT1, stearyl-CoA desaturase-1, TERT, TGF-beta-1, TGF-beta-IR1, Topoisomerase I, Topoisomerase II, VEGF, VEGFR1, VEGFR2, VLA1, VLA4, and vanilloid receptor (VR1).